

### **REMARKS**

Claims 1-9, 12 and 13 are currently pending in the instant application. Claims 1-9 have been amended. Claim 8 has been amended to correct dependency on multiple claim 7. New claim 12 contains the deleted subject matter of claim 8. Claim 9 has been amended to correct dependency on multiple claim 7. New claim 13 contains the deleted subject matter of claim 9. Claims 10 and 11 have been canceled.

No new matter has been added. In light of the above amendments, claims 1-9, 12 and 13 are under active consideration in this application.

### **Priority**

The instant application is the national stage of International Application PCT/EP00/05547 (WO 00/78735) filed on June 16, 2000 which claims benefit to prior U.S. Provisional Application 60/146,644, filed July 30, 1999 and prior German Application Nos. DE 199 28 281 and DE 100 23 085, filed June 21, 1999 and May 11, 2000, respectively. Benefit of the earlier filing date of the prior International Application was claimed pursuant to 35 U.S.C. §365(c) on the Declaration for Utility or Design Application, filed on April 25, 2002 in three counterparts, copies of which are submitted herewith. Benefit of the earlier filing date of the prior International Application was incorrectly claimed under 371 on the Application Data Sheet. A new Application Data Sheet is submitted herewith. Attorney for Applicants submits that the priority is in order and respectfully requests acknowledgement.

### **Specification**

The specification is objected to for informalities regarding the continuity information. The specification has been amended to recite:

This application is a continuation of International Application PCT/EP00/05547 (WO 00/78735) filed on June 16, 2000 which claims benefit to prior U.S. Provisional Application 60/146,644, filed July 30, 1999 and prior German Application Nos. DE 199 28 281 and DE 100 23 085, filed June 21, 1999 and May 11, 2000, respectively. Benefit of the earlier filing date of the prior International Application is hereby claimed pursuant to 35 U.S.C. § 365(c).

This objection, therefore, has been obviated.

### **Claim Objections**

Claims 8-11 are objected to as being in improper form for dependency on multiple dependent claim 7. Claims 10 and 11 have been cancelled without prejudice. Claims 8 and 9 have been amended to depend only on claims 1 to 6, thus this objection has been obviated.

### **Rejections under Section 112**

Claims 1-7 are rejected under 35 U.S.C. §112, second paragraph as being indefinite.

According to the Examiner, claims 1-5 are indefinite in the recitation “Bicyclic heterocycles of general Formula”. Applicants disagree, however, in order to advance prosecution, claims 1-5 have been amended according to the Examiner’s suggestion to recite “A quinazoline compound of Formula”. This rejection, therefore, has been overcome.

According to the Examiner, claims 1-5 are indefinite in the recitation “the tautomers, stereoisomers and salts thereof”. Applicants disagree, however, in order to advance prosecution, claims 1-5 have been amended according to the Examiner’s suggestion to recite “or the tautomers, or stereoisomers or pharmaceutically acceptable salts thereof”. This rejection, therefore, has been overcome.

According to the Examiner, claim 6 is indefinite in the recitation “as well as the salts thereof”. Applicants disagree, however, in order to advance prosecution, claim 6 has been amended according to the Examiner’s suggestion to recite “or pharmaceutically acceptable salts thereof”. This rejection, therefore, has been overcome.

According to the Examiner, claim 7 is indefinite in the recitation “Physiologically acceptable salts of the compounds...to at least one of claims...”. Applicants disagree, however, in order to advance prosecution, claim 7 has been amended according to the Examiner’s suggestion to recite “Pharmaceutically acceptable salts of the compounds...to one of claims...”. This rejection, therefore, has been overcome.

### **Rejections under Section 103**

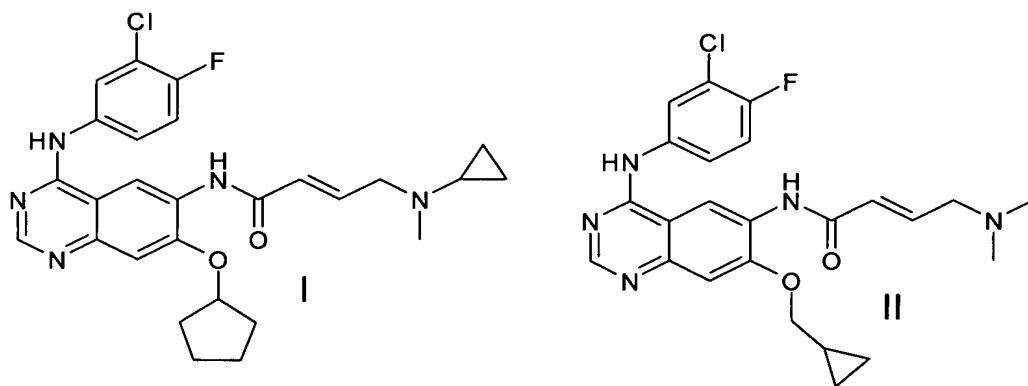
Claims 1-7 are rejected under 36 U.S.C. §103(A) as being obvious in view of Barker, EP 566226 (“the ‘226 reference”) and further in view of Bridges *et al.*, WO 9738983 (“the ‘983 reference”).

According to the Examiner, it would have been obvious to one having ordinary skill in the art at the time of the invention to select any of the species of the genus taught by the '226 reference, *i.e.*, substituted quinazoline with free 6-NH<sub>2</sub> and condense with maleic anhydride to get -NHCO-CH=CH-COOH, and to modify the end group as taught by the '983 reference.

Applicants respectfully disagree. The claims, as amended, refer only to quinazolines which are substituted in position 7 (which is R<sub>c</sub>) with cycloalkyloxy- or cycloalkylalkoxy-groups.

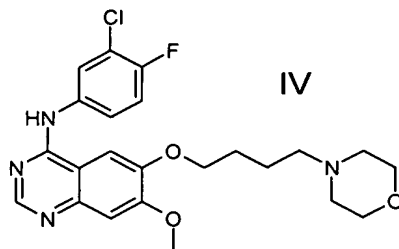
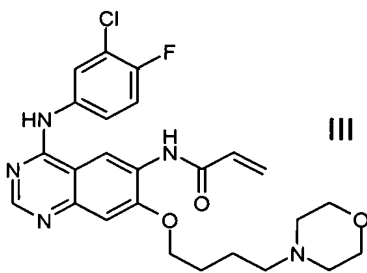
The difference of the compounds as claimed to the compounds of the '226 reference and the '983 reference cited by the Examiner is that the compounds of the present invention, in contrast to the cited state of the art, comprise only cycloalkyloxy- or cycloalkylalkoxy-groups at position 7.

Furthermore, these groups are responsible for a higher stability with regard to microsomal metabolic degradation. The half-lives of two of the compounds falling under the scope of the amended claims was evaluated in human liver microsomes. These compounds have the following formula:



The  $t_{1/2}$ -value of compound I was 30 min and for compound II it was 107 min.

Further, two compounds falling under the scope of the cited applications having the following formula were evaluated:



The  $t_{1/2}$ -value for compound III was 10 min and for compound IV it was 18 min.

In contrast to the compounds of the cited state of the art, the compounds of the present invention, having a cycloalkyloxy- or cycloalkylmethoxy-group as  $R_c$ , are much more stable with regard to microsomal metabolic degradation. This advantage cannot be derived from the cited documents. Therefore, the amended claims are not obvious in view of the prior art. This rejection under Section 103, therefore, should be withdrawn.

### CONCLUSION

In light of the above amendments and remarks, Applicants submit that all of the objections and rejections have been overcome and must be withdrawn. Further, Applicants submit that the application is now in form for issuance and an early allowance is earnestly requested. If any issues remain, the Examiner is invited to telephone the Attorney at the number below.

Respectfully submitted,

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